D
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
BO 42502		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL00/00118	24/02/2000	24/02/1999
International Patent Classification (IPC) or national classification and IPC C07C239/08		
Applicant SCA HYGIENE PRODUCTS ZEIST B.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25/09/2000	13.07.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Goetz, G Telephone No. +49 89 2399 8105

Form PCT/IPEA/409 (cover sheet) (January 1994)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-9

Claims 1-5 are directed to a process for preparing nitrosonium ions by oxidation of a nitroxyl compound in the presence of a complex of a transition metal and a complexing agent
Claims 6-9 are directed to the use of the nitrosonium compounds for the oxidation of carbohydrates prepared according to the process of claims 1-5

2. Claims: 10-14

These claims are directed to "oxidised carbohydrates"

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NL 00/00118

B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

P. NT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
BO 42502/400		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/NL 00/00118	24/02/2000	24/02/1999
Applicant		
SCA HYGIENE PRODUCTS ZEIST B.V. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

PROCESS FOR PRODUCING NITROSONIUM IONS

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

PATENT COOPERATION TREATY

PCT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

13-8-01

24-8-01

To:

JORRITSMA, Ruurd et al
NEDERLANDSCH OCTROOIBUREAU
Postbus 29720
Scheveningseweg 82
NL-2502 LS The Hague
PAYS-BAS

Nederlandsch Octrooibureau
INGEK. 18 JUL 2001
Paraaf Bewerken

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

	Date of mailing *(day/month/year)* 13.07.2001
Applicant's or agent's file reference BO 42502 - RJ	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL00/00118	24/02/2000	24/02/1999

Applicant
SCA HYGIENE PRODUCTS ZEIST B.V. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Pfitzner, G Tel.+49 89 2399-8032

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
JORRITSMA, Ruurd et al
NEDERLANDSCH OCTROOIBUREAU
Postbus 29720
Scheveningseweg 82
NL-2502 LS The Hague
PAYS-BAS

8-3-01

8-5-01

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	08.02.2001
Applicant's or agent's file reference: BO 42502	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL00/00118	24/02/2000	24/02/1999

International Patent Classification (IPC) or both national classification and IPC
C07C239/08

Applicant
SCA HYGIENE PRODUCTS ZEIST B.V. et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 24/06/2001.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
Goetz, G

Formalities officer (incl. extension of time limits)
Roche, S
Telephone No. +49 89 2399 8031

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-8 as originally filed

Claims, No.:

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:
   see separate sheet

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrialapplicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	6-9,10-14
Inventive step (IS)	Claims	
Industrial applicability (IA)	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item IV

Lack of unity of invention

1. The application lacks unity in the sense of Rule 13 PCT. The two inventions in this international application, as follows (see PCT form405 "Invitation to restrict or to pay additional fees"):

   I. Claims: 1-9
   Claims 1-5 are directed to a process for preparing nitrosonium ions by oxidation of a nitroxyl compound in the presence of a complex of a transition metal and a complexing agent
   Claims 6-9 are directed to the use of the nitrosonium compounds for the oxidation of carbohydrates prepared according to the process of claims 1-5

   II. Claims: 10-14
   These claims are directed to "oxidised carbohydrates"

2. The two separate inventions are both characterized by an individual special technical feature which are not linked to form one single inventive concept.
   The problem to be solved by the first invention is the provision of a process for the preparation of nitrosonium compounds via oxidation of a nitroxyl compound. The solution is represented by performing the oxidation in the presence of complex of a transition metal and a complexing agent.
   The problem to be solved by the second invention is to be defined by the provision of "oxidised carbohydrates".
   Although these carbohydrates may be prepared by the use of nitrosonium compounds (which is well known in the art) the special technical feature of the first invention, namely the process for preparing nitrosonium ions by oxidation of a nitroxyl compound in the presence of a complex of a transition metal and a complexing agent, does not appear in any of claims 10 to 14.

A common and single inventive concept linking both subjects is thus missing. Both two different groups of inventions concern different problems which are solved by different technical unrelated procedural or structural features, so that each of the inventions is characterised by its own separate concept.

3. Since the applicant paid the additional examination fee, present Written Opinion covers all claims, namely claim 1 to 14.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1 Recl. Trav. Chim. Pays-Bas 113, 165-166 (1994) [XP000560836]
D2 WO-A-95/07303
D3 Römpp Lexikon "Übergangsmetalle"
D4: US-A-3 632 802 (BEMILLER JAMES N ET AL) 4 January 1972 (1972-01-04)
D5: US-A-5 747 658 (VEELAERT SARAH ET AL) 5 May 1998 (1998-05-05)

A. Claims 6-9:

These claims are characterised by the fact that "the nitrosonium ion is produced by the process according to any one of claims 1-5".
Such a characterization is not to be regarded as a limiting feature.
D1 as well as D2 already disclose the oxidation of a carbohydrate using TEMPO-mediated oxidation reaction. This means that nitrosonium ions are present.
All features of claims 6-9 are thus well-known in the art (see D1 and D2). For the novelty of the claimed process it is irrelevant, if the nitrosonium is produced in a specific or different way.
Therefore claims 6 to 9 in their present form are not novel with respect to said

prior art (Article 33.2 PCT).

B. Claims 10-14:

D4 as well as D5 (see the passages cited in the Intern. search Report) disclose compounds falling within the scope of present claims.
Therefore claims 10 to 14 are not novel with respect to said prior art (Article 33.2 PCT).

Re Item VIII
Certain observations on the international application

1. The definition of "transition metal" is not unambiguously clear (see D3).
Having regard to D3 it appears that in particular the elements Zn, Cd and Hg do not fall within the definition of "transition metals" according to IUPAP.
Clarification seems necessary.

CHAPTER II

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No.	PCT/NL00/00118
Applicant's or agent's file reference	BO 42502

For International Preliminary Examining Authority use only

Date stamp of the IPEA

Applicant

SCA Hygiene Products Zeist B.V.

Calculation of prescribed fees

1. Preliminary examination fee	EUR 1533	P
2. Handling fee *(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)*	EUR 148	H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	EUR 1681	TOTAL

Mode of Payment

[X]	authorization to charge deposit account with the IPEA (see below)	[ ]	cash
[ ]	cheque	[ ]	revenue stamps
[ ]	postal money order	[ ]	coupons
[ ]	bank draft	[ ]	other *(specify)*:

Deposit Account Authorization *(this mode of payment may not be available at all IPEAs)*

The IPEA/ /EP [ ] is hereby authorized to charge the total fees indicated above to my deposit account.

[X] *(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

28 09 0001	25 September 2000	F.H.J.F. Janssen
Deposit Account Number	Date *(day/month/year)*	Signature

International application No.
PCT/NL00/00118

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:			For International Preliminary Examining Authority use only: received	not received
1. translation of international application	:	sheets	☐	☐
2. amendments under Article 34	:	sheets	☐	☐
3. copy (or, where required, translation) of amendments under Article 19	:	sheets	☐	☐
4. copy (or, where required, translation) of statement under Article 19	:	sheets	☐	☐
5. letter	:	sheets	☐	☐
6. other *(specify)*	:	sheets	☐	☐

The demand is also accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ nucleotide and or amino acid sequence listing in computer readable form
6. ☐ other *(specify)*:

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

Nederlandsche Octrooibureau

A. van Westenbrugge

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):
3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. ☐ The applicant has been informed accordingly.
4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

International application No.
PCT/NL00/00118

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is [X] agent [ ] common representative

[X] has been appointed earlier and represents the applicant(s) also for international preliminary examination.

[ ] is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

[ ] is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Jorritsma, Ruurd et al.
Nederlandsch Octrooibureau
Scheveningseweg 82 (P.O. Box 29720)
2502 LS The Hague
The Netherlands

Telephone No.: +31-70-352 75 00

Facsimile No.: +31-70-352 75 28

Teleprinter No.:

[ ] **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special addr ess to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

1. The applicant wishes the international preliminary examination **to start on the basis of:**

[X] the international application as originally filed

the description
- [ ] as originally filed
- [ ] as amended under Article 34

the claims
- [ ] as originally filed
- [ ] as amended under Article 19 (together with any accompanying statement)
- [ ] as amended under Article 34

the drawings
- [ ] as originally filed
- [ ] as amended under Article 34

2. [ ] The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. [ ] The applicant wishes the start of the international preliminary examination **to be postponed** until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: .....

- [ ] which is the language in which the international application was filed.
- [ ] which is the language of a translation furnished for the purposes of international search.
- [ ] which is the language of publication of the international application.
- [ ] which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby **elects all eligible States** *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes **not to elect:**

International application No.
PCT/NL00/00118

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Jaschinski, Thomas
Elfenstrasse 46
D-68169 Mannheim
Germany

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
Germany (DE)	Germany (DE)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Van den Dool, Ronald Tako Marinus
Dalkruid 1
NL-4102 KR Culemborg
The Netherlands

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
The Netherlands (NL)	The Netherlands (NL)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

☐ Further applicants are indicated on another continuation sheet.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ /EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND

Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION

Applicant's or agent's file reference: BO 42502

International application No.	International filing date *(day/month/year)*	(Earliest) Priority date *(day/month/year)*
PCT/NL00/00118	24 February 2000 (24.02.00)	24 February 1999 (24.02.99)

Title of invention: Process for producing nitrosonium ions

Box No. II APPLICANT(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

SCA Hygiene Products Zeist B.V.
P.O. Box 360
NL-3700 AJ Zeist
The Netherlands

Telephone No.:

Facsimile No.:

Teleprinter No.:

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
The Netherlands (NL)	The Netherlands (NL)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Besemer, Arie Cornelis
H. v.d. Boschstraat 111
NL-3958 CC Amerongen
The Netherlands

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
The Netherlands (NL)	The Netherlands (NL)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Jetten, Jan Matthijs
Costerlaan 3 B
NL-3701 JL Zeist
The Netherlands

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
The Netherlands (NL)	The Netherlands (NL)

[X] Further applicants are indicated on a continuation sheet.

Continuation of Box No. III **FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)**

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

JETTEN, Jan Matthijs
Costerlaan 3 B
3701 JL ZEIST
The Netherlands

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: The Netherlands (NL)

State *(that is, country)* of residence: The Netherlands (NL)

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

JASCHINSKI, Thomas
Elfenstrasse 46
D 68169 MANHEIM
Deutschland

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: Deutschland (DE)

State *(that is, country)* of residence: Deutschland (DE)

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [XX] the United States of America only
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Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

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Dalkruid 1
4102 KR CULEMBORG
The Netherlands

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: The Netherlands (NL)

State *(that is, country)* of residence: The Netherlands (NL)

This person is applicant for the purposes of:
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This person is:
- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
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- [ ] Further applicants and/or (further) inventors are indicated on another continuation sheet.

B x No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in th Supplemental B x.

Filing date f earlier application *(day/month/year)*	Number of earlier applicati n	Where earlier application is:		
		nati nal application: country	regional application:* regional Office	international applicati n: receiving Office
item (1) 24-02-1999	99200536.3	Europe		
item (2)				
item (3)				

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): _____

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

B x No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used)*:
ISA /

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority)*:

Date *(day/month/year)*	Number	Country *(or regional Office)*
29 july 1999	EP 99 20 0536	Europe

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets**:

request	:	4
description (excluding sequence listing part)	:	7
claims	:	2
abstract	:	1
drawings	:	
sequence listing part of description	:	
Total number of sheets	:	14

This international application is **accompanied by** the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify)*: Copy earlier Search report

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

VAN WESTENBRUGGE, Andries

Nederlandsch Octrooibureau, The Hague, 24 february 2000

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA /
6. ☐ Transmittal of search copy delayed until search fee is paid.

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Date of receipt of the record copy by the International Bureau:

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- ■ **AP** **ARIPO Patent:** **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **SD** Sudan, **SL** Sierra Leone, **SZ** Swaziland, **TZ** United Republic of Tanzania, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ■ **EA** **Eurasian Patent:** **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakhstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ■ **EP** **European Patent:** **AT** Austria, **BE** Belgium, **CH and LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ■ **OA** **OAPI Patent:** **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Côte d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea-Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- ■ **AE** United Arab Emirates
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- ■ **AT** Austria
- ■ **AU** Australia
- ■ **AZ** Azerbaijan
- ■ **BA** Bosnia and Herzegovina
- ■ **BB** Barbados
- ■ **BG** Bulgaria
- ■ **BR** Brazil
- ■ **BY** Belarus
- ■ **CA** Canada
- ■ **CH and LI** Switzerland and Liechtenstein
- ■ **CN** China
- ■ **CR** Costa Rica
- ■ **CU** Cuba
- ■ **CZ** Czech Republic
- ■ **DE** Germany
- ■ **DK** Denmark
- ■ **DM** Dominica
- ■ **EE** Estonia
- ■ **ES** Spain
- ■ **FI** Finland
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- ■ **HU** Hungary
- ■ **ID** Indonesia
- ■ **IL** Israel
- ■ **IN** India
- ■ **IS** Iceland
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- ■ **KE** Kenya
- ■ **KG** Kyrgyzstan
- ■ **KP** Democratic People's Republic of Korea
- ■ **KR** Republic of Korea
- ■ **KZ** Kazakhstan
- ■ **LC** Saint Lucia
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- ■ **LR** Liberia
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- ■ **LT** Lithuania
- ■ **LU** Luxembourg
- ■ **LV** Latvia
- ■ **MA** Morocco
- ■ **MD** Republic of Moldova
- ■ **MG** Madagascar
- ■ **MK** The former Yugoslav Republic of Macedonia
- ■ **MN** Mongolia
- ■ **MW** Malawi
- ■ **MX** Mexico
- ■ **NO** Norway
- ■ **NZ** New Zealand
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- ■ **TJ** Tajikistan
- ■ **TM** Turkmenistan
- ■ **TR** Turkey
- ■ **TT** Trinidad and Tobago
- ■ **TZ** United Republic of Tanzania
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- ■ **US** United States of America
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- ■ **YU** Yugoslavia
- ■ **ZA** South Africa
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Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- ☐ .....
- ☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* BO 42502/400

Box No. I TITLE OF INVENTION

Process for selective oxidation of carbohydrates

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

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The netherlands

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(that is, country)* of nationality: The Netherlands (NL)

State *(that is, country)* of residence: The Netherlands (NL)

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

BESEMER, Arie Cornelis
H. v.d.Boschstraat 111
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The Netherlands

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: The Netherlands (NL)

State *(that is, country)* of residence: The Netherlands (NL)

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ■ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

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NL-2502 LS THE HAGUE
THE NETHERLANDS

Telephone No. 70 3527500

Facsimile No. 70 3527528

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

this solution 25 mg manganese nitrate was added, followed by 100 µl of hydrogen peroxide (3% solution, w/w) and bipyridine solution (5 ml 0.05 M). The reaction was conducted at pH 6.5. At the first day 60 mg (1.8 mmol) hydrogen peroxide was added and after one day 25 mg of uronic acid was formed. During the second day 30 mg hydrogen peroxide was added and the amount of uronic acid was increased to 50 mg. The aldehyde groups were converted into carboxylic acid groups with hydrogen peroxide/sodium chlorite the content raised to 90 mg. (D.O. 60%). This example shows that higher levels of oxidising agent and longer reaction times lead to higher yields, compared to example 4.

Example 6: *Oxidation of pullulan with TEMPO / Mn / oxygen*

[0025] To a solution of 400 mg pullulan in 25 ml water 50 mg TEMPO, 180 mg manganese nitrate and 10 ml 0.05 M bipyridine were added. The pH was brought to 9 and oxygen gas was bubbled through the solution. A fast decrease in pH was observed. By addition of sodium hydroxide the pH of the solution was kept at 9. After one night of reaction the uronic acid content of the reaction mixture was determined according to the Blumenkrantz method 20 % of uronic acid was formed.

Example 7: *Oxidation of α-methylglucopyranoside with hydrogen peroxide, cobalt chloride (II)and bipyridine.*

[0026] To a solution of 80 mg α-methylglucopyranoside and 25 mg TEMPO in 5 ml water, 2 ml of a 0.08M cobalt(II) chloride solution and 4 ml bipyridine solution were added. After adjusting the pH by addition of 0.05 M NaOH to 7, 50 ml hydrogen peroxide solution (3% w/w) was added. This resulted in a pH drop followed (usually after 10 to 15 minutes) by an increase When the pH was at its original value again, 50 ml hydrogen peroxide was added. In total 350 ml was added. After standing for one night the pH was brought to 3.5 and 100ml hydrogen peroxide (30% w/w) and 100 mg sodium chlorite (Aldrich 80% purity) were added. After reacting for two hours the uronic acid content was determined. According to the Blumenkrantz method, before subsequent oxidation 9% and thereafter 12 % uronic acid was formed.

Example 8: *A solution of 30 mmol Cobalt (II) chloride, 60 mmol bipyridine, 450 mg pullulan and 25 mg TEMPO was exposed to oxygen in a closed system.*

[0027] A reaction to at least 20% conversion proceeds as follows from the oxygen

consumption (measured with a gas burette; the rate is 3 ml per hour).

5

Claims

1. A process for producing nitrosonium ions by oxidising a nitroxyl compound with an oxidising agent, *characterised* in that the nitroxyl compound is oxidised in the presence of a complex of a transition metal and a complexing agent.

2. A process according to Claim 1, wherein a the nitroxyl compound is a di-tert-nitroxyl compound, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO).

3. A process according to Claim 1 or 2, wherein the transition metal is manganese, iron, cobalt, nickel, copper or vanadium.

4. A process according to any one of Claims 1-3, wherein the complexing agent is a nitrogen-containing compound.

5. A process according to Claim 4, wherein the complexing agent is a bipyridyl or a triazonane or a (poly)histidine.

6. A process for oxidising a carbohydrate with an oxidising agent in the presence of a nitrosonium ion as a catalyst, *characterised* in that the nitrosonium ion is produced by the process according to any one of Claims 1-5.

7. A process according to Claim 6, wherein the carbohydrate is an α-glucan or fructan or a derivative thereof .

8. A process according to any one of Claims 1-7, wherein a carbonyl-containing carbohydrate containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule is produced.

9. A process according to any one of Claims 1-8, wherein the carbohydrate is a hydroxyalkylated carbohydrate or a glycoside.

10. An oxidised carbohydrate, the carbohydrate being selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule or a chemical derivative thereof.

11. An oxidised carbohydrate according to Claim 10, containing at least 5 mono-

saccharide units per average molecule.

12. A carbohydrate derivative according to Claim 10 or 11, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -CH=N-R or -CH_2-NHR, wherein R is hydrogen, hydroxyl, amino, or a group R^1, OR^1 or NHR^1, in which R^1 is C_1-C_{20} alkyl, C_1-C_{20} acyl, a carbohydrate residue, or group coupled with or capable of coupling with a carbohydrate residue.

13. A carbohydrate derivative according to Claim 10 or 11, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -$CH(OR^3)$-O-CH_2-$COOR^2$ or -$CH(-O-CH_2-COOR^2)_2$, in which R^2 is hydrogen, a metal cation or an optionally substituted ammonium group, and R^3 is hydrogen or a direct bond to the oxygen atom of a dehydrogenated hydroxyl group of the carbohydrate.

14. A carbohydrate according to any one of Claims 10-13, further containing carboxyl and/or carboxymethyl groups.

The claimed novel carbohydrate oxidation products (Claims 10 to 14) can be used as thickeners, viscosifiers etc. due to their modified properties. there is no hint to be found that would render the claimed compounds obvious over said prior art.

The subject matter of claims 1 to 14 is thus regarded to be novel over said prior art (Article 33.3 PCT).

3. Industrial applicability can be acknowledged as well (Article 33.4 PCT).

Re Item VIII

Certain observations on the international application

1. The definition of "transition metal" is not unambiguously clear (see D3). Having regard to D3 it appears that in particular the elements Zn, Cd and Hg do not fall within the definition of "transition metals" according to IUPAP. Clarification seems necessary.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1 Recl. Trav. Chim. Pays-Bas 113, 165-166 (1994) [XP000560836]
D2 WO-A-95/07303
D3 Römpp Lexikon "Übergangsmetalle"
D4: US-A-3 632 802 (BEMILLER JAMES N ET AL) 4 January 1972 (1972-01-04)
D5: US-A-5 747 658 (VEELAERT SARAH ET AL) 5 May 1998 (1998-05-05)

1. The subject matter of present claims 1 to 9 is characterized by the oxidation reaction as claimed in claim 1 whereby the nitroxyl compound is oxidised in the presence of a complex of a transition metal and a complexing agent.
This characterizing feature is not disclosed in any of the available prior art documents (see D1, D2).
The oxidised carbohydrates according to present claims 10 to 14 which are characterised by the given specific substituents are not disclosed in any of the prior art documents D4 or D5.
The subject matter of claims 1 to 14 is thus regarded to be novel over said prior art (Article 33.2 PCT).

2. The process as claimed in present claims 1 to 9 is characterised by the presence of a transition metal and a complexing agent. These characterizing features are not rendered obvious from any of the prior art documents. It has further the advantage that oxidising agents based on chlorine or hydrogen peroxide can be avoided and that the oxidation reaction can be performed under mild reaction conditions. The claimed process can thus be used for modifying carbohydrates to change their physical or chemical properties.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

F ENT COOPERATION TREA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 24 October 2000 (24.10.00)	
International application No. PCT/NL00/00118	**Applicant's or agent's file reference** BO 42502/400
International filing date (day/month/year) 24 February 2000 (24.02.00)	**Priority date** (day/month/year) 24 February 1999 (24.02.99)
Applicant BESEMER, Arie, Cornelis et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

25 September 2000 (25.09.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer S. Mafla
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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Nederlandsch Octrooibureau
Anno 1888

Octrooigemachtigden
European Patent Attorneys

Merken- & Modellen-
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2280 HV RIJSWIJK

Your ref. -
Our ref. BO 42502 RJ/MM

The Hague, 3 May 2001

Re: International Patent Application PCT/NL00/00118
Applicant: SCA Hygiene Products Zeist B.V. et al.

Dear Sirs,

In response to the Written Opinion dated 8 February 2001, substitute sheets for pages 7-10 are filed, together with the following comments.

Amended claims:
The replacement of pages 7 and 8 only serves to adjust the layout of example 8, as according to e.g. example 6, without any substantive amendment. In the claims (pages 9 and 10) claims 10 and 11 have been restricted according to previous claim 14. Claim 12 and 13 have been reworded so as to maintain the original scope, with deletion of the dependence on claims 10 and 11.

Novelty:
No novelty objections were raised against claims 1-5.

Claims 6-9 were held to be novel on the basis that the feature "a nitrosonium ion is produced by the process according to anyone of claims 1-5" would not be a limiting feature. However, it is stressed that this feature is presented as a process step, in particular as it is the characterising step of the process claim. Therefore it must be regarded as a limiting feature.

Although perhaps unnecessary, it is pointed out that neither D1 nor D2 teaches the oxidation of a carbohydrate using a nitroxyl compound in the presence of a complex of a transition metal and a complexing agent.

Claims 10-14 were objected to as not being novel over D4 and D5. First of all, it is noted that the amino derivatives and ketal derivatives of claims 12 and 13, respectively, are not mentioned or suggested in D4 or D5 or any other piece of prior art, and are

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therefore clearly novel. No argument has been presented against this novelty.

Claim 10 has now been restricted in that in addition to the aldehyde groups, carboxyl groups and/or carboxy metal groups should be present. D4 teaches the oxidation of carbohydrates using potassium ferrate. It is stated explicitly, column 2, line 58, that this oxidation occurs without the formation of carboxyl groups. Therefore, the products of claims 10 and 11 are novel over this prior art. D5 is concerned with the production of dialdehyde carbohydrates, i.e. carbohydrates wherein the cyclic vicinal diol is oxidised to an acyclic dialdehyde (see e.g. the equation in col. 1, l. 39). It is commonly known that periodate oxidation of carbohydrates exclusively results in this type of ring-opened dialdehydes. Present claim 10 requires that the carbaldehyde group is present on a cyclic monosaccharide chain group and is, for that reason already, distinguished from D5. Thus, claims 10, 11 and 14 as amended, are also novel.

The applicant believes that the claims as now presented are also inventive over the cited prior art.

It is requested that, in case objections as to novelty and, especially, inventive step would subsist against the current claims, a further opportunity for comment or amendment be given before the issuance of the International Preliminary Examination Report. This seems to be especially appropriate as two examination fees have been paid, and only rough novelty objections and no inventive step assessment have been made yet.

The agent,

R. Jorritsma

Encl.: substitute pates for pages 7-10

this solution 25 mg manganese nitrate was added, followed by 100 µl of hydrogen peroxide (3% solution, w/w) and bipyridine solution (5 ml 0.05 M). The reaction was conducted at pH 6.5. At the first day 60 mg (1.8 mmol) hydrogen peroxide was added and after one day 25 mg of uronic acid was formed. During the second day 30 mg hydrogen peroxide was added and the amount of uronic acid was increased to 50 mg. The aldehyde groups were converted into carboxylic acid groups with hydrogen peroxide/sodium chlorite the content raised to 90 mg. (D.O. 60%). This example shows that higher levels of oxidising agent and longer reaction times lead to higher yields, compared to example 4.

Example 6: *Oxidation of pullulan with TEMPO / Mn / oxygen*

[0025] To a solution of 400 mg pullulan in 25 ml water 50 mg TEMPO, 180 mg manganese nitrate and 10 ml 0.05 M bipyridine were added. The pH was brought to 9 and oxygen gas was bubbled through the solution. A fast decrease in pH was observed. By addition of sodium hydroxide the pH of the solution was kept at 9. After one night of reaction the uronic acid content of the reaction mixture was determined according to the Blumenkrantz method 20 % of uronic acid was formed.

Example 7: *Oxidation of α-methylglucopyranoside with hydrogen peroxide, cobalt chloride (II) and bipyridine.*

[0026] To a solution of 80 mg α-methylglucopyranoside and 25 mg TEMPO in 5 ml water, 2 ml of a 0.08M cobalt(II) chloride solution and 4 ml bipyridine solution were added. After adjusting the pH by addition of 0.05 M NaOH to 7, 50 ml hydrogen peroxide solution (3% w/w) was added. This resulted in a pH drop followed (usually after 10 to 15 minutes) by an increase When the pH was at its original value again, 50 ml hydrogen peroxide was added. In total 350 ml was added. After standing for one night the pH was brought to 3.5 and 100ml hydrogen peroxide (30% w/w) and 100 mg sodium chlorite (Aldrich 80% purity) were added. After reacting for two hours the uronic acid content was determined. According to the Blumenkrantz method, before subsequent oxidation 9% and thereafter 12 % uronic acid was formed.

Example 8: *Oxidation of pullulan with TEMPO / Co / oxygen*

[0027] A solution of 30 mmol cobalt (II) chloride, 60 mmol bipyridine, 450 mg pullulan and 25 mg TEMPO was exposed to oxygen in a closed system. A reaction to at

least 20% conversion proceeds, as follows from the oxygen consumption (measured with a gas burette; the rate is 3 ml per hour).

Claims

1. A process for producing nitrosonium ions by oxidising a nitroxyl compound with an oxidising agent, *characterised* in that the nitroxyl compound is oxidised in the presence of a complex of a transition metal and a complexing agent.

2. A process according to Claim 1, wherein a the nitroxyl compound is a di-tert-nitroxyl compound, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO).

3. A process according to Claim 1 or 2, wherein the transition metal is manganese, iron, cobalt, nickel, copper or vanadium.

4. A process according to any one of Claims 1-3, wherein the complexing agent is a nitrogen-containing compound.

5. A process according to Claim 4, wherein the complexing agent is a bipyridyl or a triazonane or a (poly)histidine.

6. A process for oxidising a carbohydrate with an oxidising agent in the presence of a nitrosonium ion as a catalyst, *characterised* in that the nitrosonium ion is produced by the process according to any one of Claims 1-5.

7. A process according to Claim 6, wherein the carbohydrate is an α-glucan or fructan or a derivative thereof .

8. A process according to any one of Claims 1-7, wherein a carbonyl-containing carbohydrate containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule is produced.

9. A process according to any one of Claims 1-8, wherein the carbohydrate is a hydroxyalkylated carbohydrate or a glycoside.

10. An oxidised carbohydrate, the carbohydrate being selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule or a chemical derivative thereof, and further containing carboxyl and/or carboxymethyl groups.

11. An oxidised carbohydrate according to Claim 10, containing at least 5 monosaccharide units per average molecule.

12. A carbohydrate derivative selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -CH=N-R or $-CH_2-NHR$, wherein R is hydrogen, hydroxyl, amino, or a group R^1, OR^1 or NHR^1, in which R^1 is C_1-C_{20} alkyl, C_1-C_{20} acyl, a carbohydrate residue, or group coupled with or capable of coupling with a carbohydrate residue.

13. A carbohydrate derivative selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula $-CH(OR^3)-O-CH_2-COOR^2$ or $-CH(-O-CH_2-COOR^2)_2$, in which R^2 is hydrogen, a metal cation or an optionally substituted ammonium group, and R^3 is hydrogen or a direct bond to the oxygen atom of a dehydrogenated hydroxyl group of the carbohydrate.

14. A carbohydrate according to Claim 12 or 13, further containing carboxyl and/or carboxymethyl groups.

PROCESS FOR PRODUCING NITROSONIUM IONS

[0001] The invention relates to the production of nitrosonium ions (oxoammonium ions) by oxidation of nitroxyl radicals, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO). The nitrosonium ions can be used as a catalytic oxidising agent for the selective oxidation of primary alcohols to aldehydes.

[0002] Such a process in which TEMPO is reoxidised by chemical means is known from a review by De Nooy in *Synthesis* 1996, 1153-1174 and from WO 95/07303.

[0003] It was found according to the invention that oxidation of alcohol functions, especially primary alcohol functions, using nitrosonium ions, can be carried out without using chlorine-based oxidising agents and with the use of hydrogen peroxide or oxygen as the ultimate oxidising agent. The oxidation according to the invention is performed using transition complexes of a transition metal and a complexing agent as intermediate oxidants. This oxidation, when carried out on primary alcohols, results in the formation of aldehydes. The aldehydes may be present in the (hemi)acetal form and related structures. The process is particularly suitable for oxidising carbohydrates having primary alcohol functions. An adaptation of the oxidation of the invention can be used to oxidise secondary alcohols, especially carbohydrates, to keto derivatives. The process of the invention is further defined by the characterising features of the appending claims.

[0004] In the following description, reference is made to TEMPO only for the sake of simplicity, but it should be understood that other suitable nitroxyls, i.e. organic nitroxyl compounds lacking α-hydrogen atoms, such as 2,2,5,5-tetramethylpyrrolidine-N-oxyl (PROXYL), 4-hydroxy-TEMPO, 4-acetamido-TEMPO and derivatives thereof and those described in WO 95/07303 can be substituted for TEMPO. These di-tert-alkyl nitroxyls are especially suitable for selectively oxidising primary alcohols to aldehyde functions, in particular in the presence of secondary alcohol functions that should not be oxidised. Less sterically hindered nitroxyls, such as 4,4-dimethyloxazolidine-N-oxyl (DOXYL), are suitable for preferentially oxidising secondary alcohols to keto functions, for example in the production of keto starch. The active oxidising species is the nitrosonium ion (oxo-ammonium ion $>N^{+}=O$), that is produced in situ by oxidation of the corresponding hydroxylamine and nitroxyl radical. If desired, the reaction can be performed in two steps, the production of the nitrosonium ion being the first and the oxidation of the alcohol function being the second.

[0005] A catalytic amount of nitroxyl is preferably 0.1-25 % by weight, based on the primary alcohol, or 0.1-25 mol% with respect to the primary alcohol. The nitroxyl may also be immobilised, e.g. by coupling of the hydroxyl group of 4-hydroxy-TEMPO to a suitable

carrier, or in the form of a polymeric nitroxyl such as:
-[$(CH_3)_2$C-NO.-C$(CH_3)_2$-A-]$_n$-, wherein A may be an alkylene group and/or a heteroatom, and n is a number form e.g. 10 up to several hundreds.

[0006] The process of the invention results in oxidation of primary alcohols initially to the corresponding aldehydes. If required the primary products can be further oxidised to the corresponding carboxylic acids by using known oxidising agents such as hypochlorite, chlorite, hydrogen peroxide or by using TEMPO-mediated oxidation under more vigorous conditions such as an increased temperature e.g. from 40-80 °C, or for prolonged exposure to the reaction conditions. Alternatively, the aldehyde/carboxylic acid ratio can be increased by using relative low pH's (e.g. pH 3-7), by controlled addition of oxidising agent, by lowering the oxygen concentration, or by first preparing the nitrosonium ion solution (two-step process).

[0007] The present process is especially favourable for the selective oxidation of primary hydroxyl groups in alcohols having a secondary alcohol function in addition to the primary alcohol, such as 1,6-octanediol, 1,9-octadecanediol, steroid hormones, sugar alcohols, glycosides (flavour precursors), and in particular carbohydrates having primary alcohol functions. The carbohydrates may be monosaccharides, such as glucose, fructose, disaccharides, such as sucrose, maltose, lactose, oligosaccharides and polysaccharides. The oligo- and polysaccharides may be of any type, e.g. glucans such as starch, starch components (i.e. amylose, amylopectin, dextrins), pullulan (α-1,4-α-1,4-α-1,6-glucan), chitin, lichenin etc., furanofructans such as inulin and levan, galactans, arabinogalactans, furanoid pentosans (xylans), (galacto)mannans (guar, locust bean gum), bacterial exo-polysaccharides (EPS) and the like and derivatives of such carbohydrates, such as hydrolysates. These oligo- and polysaccharides include heterosaccharides, i.e. those which have different structural units, even if those different units themselves may not have primary hydroxyl groups such as uronic acid units, e.g. in xanthan and carbohydrates derived form algae. The carbohydrates to be oxidised according to the invention include glycosides and other protected carbohydrates. Further examples are glyconic acids, such as lactobionic acid delta-lactone, that can be oxidised to glycaric acids and the like.

[0008] A distinct group of compounds suitable for oxidation with the present process consists of hydroxyalkylated carbohydrates such as hydroxypropyl starch or hydroxyethyl inulin, which result in an alternative way for producing formylalkyl carbohydrates. Other suitable carbohydrate substrates in which at least a part of the (6-) hydroxymethyl groups are intact, include for example (2- and 3-) carboxymethyl carbohydrates.

[0009] The oxidation of carbohydrates containing primary hydroxyl groups results in the corresponding carbohydrates containing aldehydes and, if desired, to carboxylic acids, with

intact ring systems. Examples include α-1,4-glucan-6-aldehydes, β-1,4-glucan-6-aldehydes, β-2,1-fructan-6-aldehydes and β-2,6-fructan-1-aldehydes. These products are useful intermediates for functional carbohydrates wherein the aldehyde groups are further reacted with e.g. amine compounds and the like. They are also useful intermediates for crosslinked carbohydrates, in which the aldehyde groups are further reacted with e.g. diamine reagents.

[0010] The catalysts to be used according to the invention are complexes of transition metals, i.e. coordination compounds between a transition metal and an organic molecule as a complexing agent having one or more free electron pairs, especially nitrogen compounds. Suitable nitrogen compounds include amino acids, phenanthrolines and other polyamines. A polyamine, which forms a complex with the transition metal, is understood to refer to compounds which comprise at least two amine nitrogen atoms, separated by at least two carbon atoms. Preferably, the polyamines comprise at least three nitrogen atoms which in each case are separated by two or more, in particular two or three, more in particular two, carbon atoms. The remaining valencies of the nitrogen atoms are preferably bound with small alkyl groups, in particular methyl. It is also possible for the polyamines to have ether or alcohol functions. The polyamines can be linear or cyclic. The polyamines should be alkaline, i.e. should not contain acid functions. Examples of polyamines which can be employed are 2,2'-bipyridyl, 2,2'-bipyrrole, 2-(dimethylaminomethyl)pyridine, tetramethylethylenediamine, pentamethyldiethylenetriamine, 1,4-dimethylpiperazine, 1,4,7-trimethyl-1,4,7-triazonane (= triazacyclononane), 1,4,7-trimethyl-1,4,7-triazecane, 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclododecane, 1,2-bis(4-methyl-1-piperazinyl)-ethane, 1,2-bis(4,7-dimethyl-1,4,7-triazonan-1-yl)ethane, and the corresponding compounds wherein one or more of the said methyl groups have been replaced by, for example, ethyl groups. It is also possible to use porphin and other porphyrins and corresponding macrocyclic polyamine compounds. Histidine and comparable amino acids having an additional nitrogen atom, and their oligopeptides such as histidyl-histidine, are other examples of suitable complexing agents. Preference is given to compounds of the bipyridyl type, triazonane type and to amines whose remaining valencies are linked to methyl groups. The counterions required for neutrality of the complexes may be common, preferably non-toxic counterions such as oxide, halide, perchlorate, acetylacetonate, nitrate, sulphate and the like.

[0011] Transition metals to be used in the metal complexes include especially those of the fourth period of the periodic table of elements from vanadium to zinc, preferably manganese, iron, cobalt, nickel and copper, in particular manganese, iron, cobalt and copper. The corresponding metals from the higher periods may also be used, such as in

particular ruthenium. The metal complexes require hydrogen peroxide, alkyl and ar(alk)yl hydroperoxides (such as tert-butyl hydroperoxide), oxygen or chlorite as an ultimate electron acceptor. About one metal atom to two to four nitrogen atoms of the complexing agent can suitably be used.

[0012] The metal complex may be used in a catalytic amount, e.g. in about an equimolar amount with respect to the nitroxyl compound. Suitable amounts of metal complexes are for example 1-25 mol% with respect to the alcohol to be oxidised.

[0013] The process of the invention can be performed under relatively mild conditions, e.g. at a pH between 5 and 10, and at a temperature between 15 and 60°C (both depending on the particular metal complex). The reaction medium can be an aqueous medium, or a homogeneous mixed medium, e.g. of a mixture of water and a secondary or tertiary alcohol or an ether/water mixture, or a heterogeneous medium, e.g. a mixture of water and a water-immiscible organic solvent such as a hydrophobic ether, a hydrocarbon or a halogenated hydrocarbon. In the latter case, the metal complex and/or the nitroxyl and the oxidising agent may be present in the aqueous phase and the alcohol substrate and the aldehyde or ketone product may be present in the organic phase. If necessary, a phase transfer catalyst may be used. The reaction medium can also be a solid/liquid mixture, in particular when the nitroxyl is immobilised on a solid carrier. A heterogeneous reaction medium may be advantageous when the substrate or the product is relatively sensitive or when separation of the product from the other reagents may present difficulties.

[0014] The invention also pertains to novel carbohydrate oxidation products and derivatives thereof, which can be obtained with the process of the invention. These include polysaccharides in which at least 1 hydroxymethyl per 100, especially per 50 or even per 25, monosaccharide units has been converted to a carbaldehyde group, whether or not in hemiacetal or similar form, with the proviso that on average each molecule contains at least 1 carbaldehyde group other than a possible (hemiacetalised) aldehyde group at the reducing end of an oligo- or polysaccharide. When the carbohydrate is starch, the degree of oxidation is at least one carbaldehyde group per 25 anhydroglucose units. The carbaldehyde group is preferably present in chain (backbone) units, rather than in branch or terminal units. The novel products include glycoside derivatives, i.e. products which, in addition to an acetalised end group have at least one carbaldehyde group obtainable by oxidation of non-galactose hydroxymethylene groups. In the products of the invention, the monosaccharide rings that carry the carbaldehyde group are largely intact. The only common carbohydrate derivatives having a predominant content of aldehyde groups are periodate-type oxidation products of starch, cellulose and the like, in which the rings bearing the aldehyde groups are broken. The aldehyde carbohydrates covered by the

present invention are especially of types other than the cellulose or pentosan type (or derivatives such as carboxymethylated, alkylated, hydroxyalkylated cellulose). The products obtainable according to the invention may contain, in addition to the aldehyde groups, other functional groups, especially carboxyl groups obtained by further oxidation or by carboxyalkylation.

[0015] The novel derivatives of the invention are very suitable as thickeners, viscosifiers, stabilisers, wet strength additives, water-absorbing polymers and the like, and especially as starting materials for further functionalisation, especially with alcohols, amines, and other agents capable of coupling with an aldehyde function. Such agents include crosslinking agents (diamines, diols and the like), which can be used to crosslink the carbohydrates or to couple them to amino acids, proteins, active groups etc.

[0016] The process of the invention can also advantageously be used for modifying biopolymers such as starch, non-wood cellulose to allow derivatisation or to adapt viscosity and other physical or chemical properties such as (textile) strength, dyeability, etc.

[0017] The invention also pertains to derivatives obtained by coupling of the aldehyde carbohydrates described above with e.g. amines, especially by reductive amination, to produce imino or amino derivatives of carbohydrates as defined in the appending claims. Also, the aldehyde carbohydrates can be reacted acetalised with hydroxy-functionalised compounds, e.g. glycolic acid, for further derivatisation.

Examples: *General*

[0018] Uronic acid (6-COOH of hexopyranose units) contents were determined using the Blumenkrantz et al. method (*Anal. Biochem.* (1973) **54**, 484), using boric acid (0.0125 M) in concentrated sulphuric acid, adding 3-hydroxybiphenyl and measuring the extinction at 520 nm.

[0019] Aldehyde contents were determined either by a subtractive method (determining the uronic acid content before and after of oxidation of aldehydes with chlorite and hydrogen peroxide), or by addition of hydroxylamine hydrochloride to produce an oxime and back-titration of liberated hydrochloric acid, or by ^{13}C NMR spectroscopy (intensity of C6 signal of aldehyde with respect to C1 of anhydroglucose unit, or intensity of C6 (C=N) in the oxime).

Example 1: *C6 Oxidation of methylglucopyranoside with TEMPO / Mn / hydrogen peroxide*

[0020] Sixty mg of α-methylglucopyranoside, 30 mg of Mn complex with 1,4,7-trimethyl-1,4,7-triazonane and 500 mg TEMPO (lower amounts work equally well) were

dissolved in 100 ml of demineralised water. The reaction temperature was raised to 55-60°C and the pH was maintained at 8.5. Diluted hydrogen peroxide (31 µl 30% in 10 ml demineralised water) was added over 5 h. After overnight reaction, the C6 carboxyl and C6 aldehyde contents were qualitatively shown using DIONEX HPAEC. A sample was reduced with sodium borohydride at pH 8 to confirm the presence of aldehyde functions. The carboxyl content was determined using the Blumenkrantz method to be 20%. After further oxidation of aldehyde (hemiacetal) with sodium chlorite and hydrogen peroxide, the carboxyl content was 26%. Thus the aldehyde content was 6%.

Example 2: *Oxidation of methylglucopyranoside with TEMPO / Mn / hydrogen peroxide*

[0021] To an aqueous solution of 500 mg methylglucopyranoside and 250 mg manganese (II) nitrate, 10 ml 0.05 M bipyridyl solution and 50 mg TEMPO, 0.70 ml hydrogen peroxide (3 % w/w) is added in portions of 20 µl in the course of 8 h. The pH of the mixture is kept between 6 and 7. The next day the mixture is treated with sodium chlorite to convert the aldehyde groups to carboxylic acid groups. (pH 4-5). The yield of uronic acid before and after further oxidation is 8 and 11 %, respectively.

Example 3: *C6 Oxidation of methylglucopyranoside with TEMPO / Cu / oxygen*

[0022] Sixty mg of α-methylglucopyranoside, 500 mg TEMPO and 24 mg copper / histidine complex were dissolved in 100 ml of demineralised water. The reaction temperature was maintained at 30°C and the pH was adjusted to 8.0. Oxygen was passed through the solution for two hours. After overnight reaction, the carboxyl content was determined using the Blumenkrantz method and found to be 17%.

Example 4: *Oxidation of pullulan by TEMPO / Mn / H_2O_2*

[0023] In 50 ml of water 400 mg pullulan (2.4 mmol anhydroglucose units) and 50 mg of TEMPO were dissolved. To this solution 50 mg manganese nitrate and 5 ml bipyridine 0.05 M solution were added, followed by small amounts of hydrogen peroxide. (100 µl 3% w/v per time). The pH was maintained between 6.5 and 7.0. In total 2.0 ml hydrogen peroxide (3%) was added. After one day the aldehyde groups present were converted to carboxylic acid groups by reaction with sodium chlorite/hydrogen peroxide (pH 4-5). The yield of uronic acid with respect to groups was 25%.

Example 5: *Oxidation of pullulan by TEMPO / Mn / H_2O_2*

[0024] In 25 ml of water 250 mg pullulan and 20 mg of TEMPO were dissolved. To

this solution 25 mg manganese nitrate was added, followed by 100 µl of hydrogen peroxide (3% solution, w/w) and bipyridine solution (5 ml 0.05 M). The reaction was conducted at pH 6.5. At the first day 60 mg (1.8 mmol) hydrogen peroxide was added and after one day 25 mg of uronic acid was formed. During the second day 30 mg hydrogen peroxide was added and the amount of uronic acid was increased to 50 mg. The aldehyde groups were converted into carboxylic acid groups with hydrogen peroxide/sodium chlorite the content raised to 90 mg. (D.O. 60%). This example shows that higher levels of oxidising agent and longer reaction times lead to higher yields, compared to example 4.

Example 6: *Oxidation of pullulan with TEMPO / Mn / oxygen*

[0025] To a solution of 400 mg pullulan in 25 ml water 50 mg TEMPO, 180 mg manganese nitrate and 10 ml 0.05 M bipyridine were added. The pH was brought to 9 and oxygen gas was bubbled through the solution. A fast decrease in pH was observed. By addition of sodium hydroxide the pH of the solution was kept at 9. After one night of reaction the uronic acid content of the reaction mixture was determined according to the Blumenkrantz method 20 % of uronic acid was formed.

Example 7: *Oxidation of α-methylglucopyranoside with hydrogen peroxide, cobalt chloride (II)and bipyridine.*

[0026] To a solution of 80 mg α-methylglucopyranoside and 25 mg TEMPO in 5 ml water, 2 ml of a 0.08M cobalt(II) chloride solution and 4 ml bipyridine solution were added. After adjusting the pH by addition of 0.05 M NaOH to 7, 50 ml hydrogen peroxide solution (3% w/w) was added. This resulted in a pH drop followed (usually after 10 to 15 minutes) by an increase When the pH was at its original value again, 50 ml hydrogen peroxide was added. In total 350 ml was added. After standing for one night the pH was brought to 3.5 and 100ml hydrogen peroxide (30% w/w) and 100 mg sodium chlorite (Aldrich 80% purity) were added. After reacting for two hours the uronic acid content was determined. According to the Blumenkrantz method, before subsequent oxidation 9% and thereafter 12 % uronic acid was formed.

Example 8: *A solution of 30 mmol Cobalt (II) chloride, 60 mmol bipyridine, 450 mg pullulan and 25 mg TEMPO was exposed to oxygen in a closed system.*

[0027] A reaction to at least 20% conversion proceeds as follows from the oxygen

consumption (measured with a gas burette; the rate is 3 ml per hour).

5

Claims

1. A process for producing nitrosonium ions by oxidising a nitroxyl compound with an oxidising agent, *characterised* in that the nitroxyl compound is oxidised in the presence of a complex of a transition metal and a complexing agent.

2. A process according to Claim 1, wherein a the nitroxyl compound is a di-tert-nitroxyl compound, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO).

3. A process according to Claim 1 or 2, wherein the transition metal is manganese, iron, cobalt, nickel, copper or vanadium.

4. A process according to any one of Claims 1-3, wherein the complexing agent is a nitrogen-containing compound.

5. A process according to Claim 4, wherein the complexing agent is a bipyridyl or a triazonane or a (poly)histidine.

6. A process for oxidising a carbohydrate with an oxidising agent in the presence of a nitrosonium ion as a catalyst, *characterised* in that the nitrosonium ion is produced by the process according to any one of Claims 1-5.

7. A process according to Claim 6, wherein the carbohydrate is an α-glucan or fructan or a derivative thereof .

8. A process according to any one of Claims 1-7, wherein a carbonyl-containing carbohydrate containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule is produced.

9. A process according to any one of Claims 1-8, wherein the carbohydrate is a hydroxyalkylated carbohydrate or a glycoside.

10. An oxidised carbohydrate, the carbohydrate being selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule or a chemical derivative thereof.

11. An oxidised carbohydrate according to Claim 10, containing at least 5 mono-

saccharide units per average molecule.

12. A carbohydrate derivative according to Claim 10 or 11, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -CH=N-R or -CH_2-NHR, wherein R is hydrogen, hydroxyl, amino, or a group R^1, OR^1 or NHR^1, in which R^1 is C_1-C_{20} alkyl, C_1-C_{20} acyl, a carbohydrate residue, or group coupled with or capable of coupling with a carbohydrate residue.

13. A carbohydrate derivative according to Claim 10 or 11, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -$CH(OR^3)$-O-CH_2-$COOR^2$ or -$CH(-O-CH_2-COOR^2)_2$, in which R^2 is hydrogen, a metal cation or an optionally substituted ammonium group, and R^3 is hydrogen or a direct bond to the oxygen atom of a dehydrogenated hydroxyl group of the carbohydrate.

14. A carbohydrate according to any one of Claims 10-13, further containing carboxyl and/or carboxymethyl groups.

this solution 25 mg manganese nitrate was added, followed by 100 µl of hydrogen peroxide (3% solution, w/w) and bipyridine solution (5 ml 0.05 M). The reaction was conducted at pH 6.5. At the first day 60 mg (1.8 mmol) hydrogen peroxide was added and after one day 25 mg of uronic acid was formed. During the second day 30 mg hydrogen peroxide was added and the amount of uronic acid was increased to 50 mg. The aldehyde groups were converted into carboxylic acid groups with hydrogen peroxide/sodium chlorite the content raised to 90 mg. (D.O. 60%). This example shows that higher levels of oxidising agent and longer reaction times lead to higher yields, compared to example 4.

Example 6: *Oxidation of pullulan with TEMPO / Mn / oxygen*

[0025] To a solution of 400 mg pullulan in 25 ml water 50 mg TEMPO, 180 mg manganese nitrate and 10 ml 0.05 M bipyridine were added. The pH was brought to 9 and oxygen gas was bubbled through the solution. A fast decrease in pH was observed. By addition of sodium hydroxide the pH of the solution was kept at 9. After one night of reaction the uronic acid content of the reaction mixture was determined according to the Blumenkrantz method 20 % of uronic acid was formed.

Example 7: *Oxidation of α-methylglucopyranoside with hydrogen peroxide, cobalt chloride (II) and bipyridine.*

[0026] To a solution of 80 mg α-methylglucopyranoside and 25 mg TEMPO in 5 ml water, 2 ml of a 0.08M cobalt(II) chloride solution and 4 ml bipyridine solution were added. After adjusting the pH by addition of 0.05 M NaOH to 7, 50 ml hydrogen peroxide solution (3% w/w) was added. This resulted in a pH drop followed (usually after 10 to 15 minutes) by an increase When the pH was at its original value again, 50 ml hydrogen peroxide was added. In total 350 ml was added. After standing for one night the pH was brought to 3.5 and 100ml hydrogen peroxide (30% w/w) and 100 mg sodium chlorite (Aldrich 80% purity) were added. After reacting for two hours the uronic acid content was determined. According to the Blumenkrantz method, before subsequent oxidation 9% and thereafter 12 % uronic acid was formed.

Example 8: *Oxidation of pullulan with TEMPO / Co / oxygen*

[0027] A solution of 30 mmol cobalt (II) chloride, 60 mmol bipyridine, 450 mg pullulan and 25 mg TEMPO was exposed to oxygen in a closed system. A reaction to at

least 20% conversion proceeds, as follows from the oxygen consumption (measured with a gas burette; the rate is 3 ml per hour).

Claims

1. A process for producing nitrosonium ions by oxidising a nitroxyl compound with an oxidising agent, *characterised* in that the nitroxyl compound is oxidised in the presence of a complex of a transition metal and a complexing agent.

2. A process according to Claim 1, wherein a the nitroxyl compound is a di-tert-nitroxyl compound, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO).

3. A process according to Claim 1 or 2, wherein the transition metal is manganese, iron, cobalt, nickel, copper or vanadium.

4. A process according to any one of Claims 1-3, wherein the complexing agent is a nitrogen-containing compound.

5. A process according to Claim 4, wherein the complexing agent is a bipyridyl or a triazonane or a (poly)histidine.

6. A process for oxidising a carbohydrate with an oxidising agent in the presence of a nitrosonium ion as a catalyst, *characterised* in that the nitrosonium ion is produced by the process according to any one of Claims 1-5.

7. A process according to Claim 6, wherein the carbohydrate is an α-glucan or fructan or a derivative thereof.

8. A process according to any one of Claims 1-7, wherein a carbonyl-containing carbohydrate containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule is produced.

9. A process according to any one of Claims 1-8, wherein the carbohydrate is a hydroxyalkylated carbohydrate or a glycoside.

10. An oxidised carbohydrate, the carbohydrate being selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule or a chemical derivative thereof, and further containing carboxyl and/or carboxymethyl groups.

11. An oxidised carbohydrate according to Claim 10, containing at least 5 monosaccharide units per average molecule.

12. A carbohydrate derivative selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -CH=N-R or $-CH_2-NHR$, wherein R is hydrogen, hydroxyl, amino, or a group R^1, OR^1 or NHR^1, in which R^1 is C_1-C_{20} alkyl, C_1-C_{20} acyl, a carbohydrate residue, or group coupled with or capable of coupling with a carbohydrate residue.

13. A carbohydrate derivative selected from disaccharides, oligosaccharides and polysaccharides of the α-glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula $-CH(OR^3)-O-CH_2-COOR^2$ or $-CH(-O-CH_2-COOR^2)_2$, in which R^2 is hydrogen, a metal cation or an optionally substituted ammonium group, and R^3 is hydrogen or a direct bond to the oxygen atom of a dehydrogenated hydroxyl group of the carbohydrate.

14. A carbohydrate according to Claim 12 or 13, further containing carboxyl and/or carboxymethyl groups.